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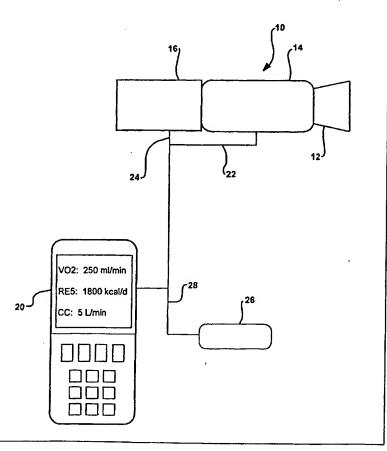
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(54) Title: AIRWAY-BASED CARDIAC OUTPUT MONITOR AND METHODS FOR USING SAME

(57) Abstract

A respiratory gas analyzer (10) for measuring the cardiac output of a subject includes a flow meter (14) and an oxygen sensor (16) interconnected with one another between a mouthpiece (12) and a source of respiratory gases which may be a controlled source or the atmosphere. An oximeter (26) provides measurements of the oxygen saturation of the subject. A computer connected to receive the signals from the flow meter (14), oxygen sensor (16), and oximeter (26) can then calculate the subject's cardiac output.



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AIRWAY-BASED CARDIAC OUTPUT MONITOR AND METHODS FOR USING SAME

Field of the Invention

The present invention relates to measurement of cardiac output of a patient. More specifically, the present invention relates to an apparatus and method for non-invasive cardiac output measurement of a subject utilizing a respiratory gas analyzer employing a flow sensor, an oxygen sensor, and a pulse oximeter which are interconnected to measure the cardiac output of the subject.

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Background of the Invention

United States Patent No. 5,836,300 to Applicant discloses a respiratory gas analyzer for measuring the metabolic activity and the cardiac output of a subject including a bi-directional flow meter and a capnometer sensor interconnected by conduits and valving between a mouthpiece and a source of respiratory gases which can be a controlled source or the atmosphere. A computer receiving signals from the flow meter and the capnometer can then calculate the subject's metabolic activity. When valving is shifted, a portion of the exhaled gases are stored in the conduit so that upon inhalation, the subject inhales a substantial portion of rebreathed gases. The computer can then calculate the patient's cardiac output as a function of the changes in total carbon dioxide content of the exhaled gas before and after the valve is shifted from a direct input to a rebreathed position and the difference in end-tidal carbon dioxide between the two positions.

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The cardiac output of a patient, that is the volume of blood ejected from the heart per unit time, is an important measured parameter in hospitalized patients. Currently, cardiac output is routinely measured by invasive techniques including thermal dilution using an indwelling pulmonary artery catheter. This technique has several disadvantages including the morbidity and mortality of placing an invasive intracardiac catheter, the infectious disease risks, significant expense and the fact that it provides an intermittent rather than a continuous measurement. A noninvasive, reusable cardiac output measurement device would substantially improve patient care and reduce hospital costs.

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The partial rebreathing technique mentioned above is a known method for cardiac output measurement. As described in Kapec and Roy, "The Noninvasive Measurement of Cardiac Output Using Partial CO₂ Rebreathing," IEEE Transactions on Biomedical Engineering, Vol. 35, No. 9, Sep. 1988, pp. 653-659, the method utilizes well known Fick procedures, substituting carbon dioxide for oxygen, and employing a sufficiently short measurement period such that venous carbon dioxide levels and cardiac output can be assumed to remain substantially constant during the measurement.

United States Patent No. 4,949,724 to Mahutte et al. discloses a method and apparatus for continuously monitoring cardiac output by utilizing a modified Fick equation. The Mahutte et al. patent replaces VO₂ in the Fick equation by VCO₂ divided by a constant representative of the gas exchange ratio of a patient in order to eliminate inaccuracies associated with monitoring the rate of uptake of oxygen.

In its original form, the Fick method of measuring cardiac output requires blood gas values for arterial and mixed venous blood as follows:

$$C.O. = VO_2/CaO_2 - C_VO_2$$

where C.O. is cardiac output, VO_2 is oxygen consumption, CaO_2 is the arterial oxygen content, and C_VO_2 is the venous oxygen content.

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By utilizing a respiratory analyzer with a fast-response oxygen sensor, the cardiac output can be determined based on the end-tidal oxygen concentration (EtO₂). End-tidal oxygen concentration is the lowest value of oxygen concentration in breath. The end-tidal oxygen concentration approximates the pulmonary capillary oxygen concentration.

Alternatively, at different points in time, it is also true that

$$C.O. = \frac{VO_{2(1)}}{CaO_{2(1)} - CvO_{2(1)}} = \frac{VO_{2(2)}}{CaO_{2(2)} - CvO_{2(2)}}.$$

If the oxygen concentration of the inspired gas is temporarily increased or decreased, the change in alveolar oxygen concentration will cause a transient uptake or release of oxygen across the pulmonary capillaries, thereby resulting in a change in the measured VO_2 and arterial oxygen content (CaO_2). If these parameters are measured during an interval of time less than the circulation time (i.e., less than approximately thirty-fifty seconds), then the venous oxygen content (C_VO_2) level remains essentially constant during this period and can be removed from the equation. Therefore, cardiac output can be determined based on the equation

$$C.O. = \frac{\Delta VO_2}{\Delta CaO_2}$$

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The use of these novel concepts in combination with the apparatus and method of the present invention therefore allows for the non-invasive measurement of cardiac output utilizing measurements of airway gases.

Summary of the Invention

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The present invention is accordingly directed toward an airway-based respiratory gas analyzer for measuring the cardiac output of a subject. In a preferred embodiment of the analyzer of the present invention, the analyzer includes a respiratory connector operative to be supported in contact with a subject so as to pass inhaled and exhaled gases as the subject breathes. A flow meter operatively connected to the respiratory connector generates electrical signals as a function of the volume of gases which pass therethrough and, in combination with the signals generated by the oxygen sensor, allow for the determination of oxygen consumption (VO₂) by integrating the flow and oxygen concentration signals over an entire breath. The oxygen sensor can also provide for the measurement of end-tidal (EtO₂) concentration. oximeter provides measurements of the subject's oxygen saturation. The computation unit receives the output signals from the flow sensor, oxygen sensor and oximeter and calculates the cardiac output based on the generated signals.

An alternative mechanism for performing measurements of the subject's cardiac output includes the subject placing the mouthpiece of the analyzer into their mouth and breathing a first oxygen concentration for a first

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period of time. Typically, the source of respiratory gases is atmospheric air. As the subject breathes, oxygen consumption (VO₂) is determined as the integral of the flow and oxygen concentration signals over the entire breath. The oximeter provides a measurement of the subject's oxygen saturation which is utilized to calculate the subject's arterial oxygen content. After obtaining the measurement of the oxygen consumption (VO₂) and arterial oxygen content (CaO₂) over the first time period, the oxygen blender is caused to provide an increase or decrease in the airway oxygen concentration of the subject for a second period of time which is less than the subject's circulation time. The oxygen consumption (VO₂) and arterial oxygen content (CaO₂) are measured over this second time period on a breath-by-breath basis and are utilized in calculating the subject's cardiac output.

Other objects, advantages and applications of the present invention will be made apparent from the following detailed description of the preferred, embodiments.

Brief Description of the Drawings

Other advantages and applications of the present invention will be made apparent by the following detailed description of preferred embodiments of the invention. The description makes reference to the accompanying drawings in which:

Figure 1 is a schematic representation of a first embodiment of the present invention;

Figure 2 is a schematic representation of a second embodiment of the present invention; and

Figure 3 is a graph of oxygen concentration over time measured in milliseconds to illustrate oxygen concentration as recorded with a fast-response oxygen sensor and is also illustrative end-tidal oxygen concentration.

Detailed Description of the Invention

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Referring to Figure 1, a preferred embodiment of the present invention includes an airway-based cardiac output analyzer, generally indicated at 10, having a mouthpiece 12, a flow sensor 14, and a gas sensor 16. The flow sensor 14 and the gas sensor 16 are disposed in fluid communication with one another.

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The mouthpiece 12 is adapted to engage the inner surfaces of a user's mouth, so as to form the sole passage for flowing respiratory gases into and out of the mouth. A nose clamp of conventional construction (not shown) can be employed in connection with the mouthpiece 12 to assure that all respiratory gas passes through the mouthpiece 12. In alternative configurations, a mask that engages the nose as well as the mouth of the user can be employed or an endotracheal tube could also be utilized.

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The mouthpiece 12 is located adjacent to a bi-directional volume flow sensor 14. The flow sensor is preferably an ultrasonic flow meter such as an ultrasonic transit time flow meter such as that manufactured by NDD Medizintechnik AG, Zurich, Switzerland, and disclosed in United States Patent Nos. 3,738,169; 4,425,805; 5,419,326; and 5,645,071. Preferably, the ultrasonic flow meter transmits and receives ultrasonic pulses along a path which is either parallel to or has a substantial component in the direction of the flow. The gas flow acts to advance or retard the flow of pulses so that the full

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transit time of the pulses is a function of the flow rate. Alternatively, the flow sensor 14 can be of the pressure differential type such as manufactured by Medical Graphics Corporation, St. Paul, Minnesota under the trademark MEDGRAPHICS and of the general type illustrated in United States Patent No. 5,038,773. Alternatively, other types of flow transducers such as pneumatics or spirometers could also be employed. The electrical output of the bi-directional flow sensor 14 is connected to a computation unit 20 through a conductive line 22.

The other end of the flow sensor 14 is connected to the gas sensor 16. The gas sensor 16 is preferably a fast-response (i.e. 50-80 millisecond response time), flow-through type oxygen sensor and is preferably of the fluorescent quench type as disclosed in United States Patent Nos. 3,725,658; 5,517,313; and 5,632,958. The preferred embodiment can employ a sensor manufactured by Sensors for Medicine and Science, Inc., Germantown, Maryland. The electrical output of the gas sensor 16 is connected to the computation unit 20 through a conductive line 24. The computation unit 20 can include a source (not shown) for directing exciting radiation to a fluorescent coating disposed on the oxygen sensor 16 and sensing the resulting fluorescence intensity which is diminished as a function of the concentration of oxygen and gas flowing over its surface to produce a direct measurement of oxygen concentration. The exciting radiation and fluorescent signal can be carried to the sensor 16 by an optical fiber (not shown).

A pulse oximeter 26 can be utilized to monitor oxygen saturation by pulse oximetry. The pulse oximeter 26 provides an output signal which is

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received by the computation unit 20 which is indicative of saturation percentage. The output signal of the pulse oximeter 26 is connected to the computational unit 20 through a conductive line 28. In a preferred embodiment, the pulse oximeter is preferably of the type manufactured by Datax-Ohmeda, Louisville, CO. Alternatively, for most healthy individuals, the pulse oximeter 26 can be omitted and the oxygen saturation can be assumed to be approximately 95-96%.

Utilizing the Fick equation in combination with the airway-based respiratory gas analyzer 10 having the flow sensor 14 and the fast-response oxygen sensor 16 allows for the determination of a subject's cardiac output by utilizing measurements of end-tidal oxygen concentration and VO_2 . The airway-based gas analyzer 10 allows for the determination of end-tidal oxygen concentration (EtO₂) as illustrated in Figure 3. If one assumes that EtO₂ \approx PvO₂ (dissolved venous oxygen concentration in the plasma), then using the PvO₂ and the hemoglobin concentration, the SvO₂ can be determined based on the oxygen dissociation curve. The pulse oximeter 26 can be used to obtain oxygen saturation movement so that based on the Fick equation of

$$C.O. = VO_2/CaO_2 - CvO_2$$

wherein VO₂ is measured by the airway based respiratory analyzer, CaO₂ and CvO₂ are determined according to the equations

$$CaO_2 = [(SaO_2)(Hgb)(1.36) + (PaO_2)(0.0031)]$$
 and

$$CvO_2 = [(SvO2)(Hgb)(1.36) + (PvO_2)(0.0031)],$$
 respectively,

wherein SaO₂ is the oxygen saturation measurement obtained by pulse oximetry, Hgb is the hemoglobin concentration (which is entered as a known

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value or by direct measurement), and PvO₂ is obtained from the measurement of EtO₂. It is assumed that EtO₂ approximates PvO₂ and, if the PvO₂ and the hemoglobin concentrations are known, using the oxygen dissociation curve, SvO₂ can be determined. The pulse oximeter 26 measures SaO₂ (alternatively, SaO₂ and PaO₂ can be reasonably assumed).

Referring to Figure 2, in an alternative embodiment of the present invention is shown wherein like numerals represent like elements among the embodiments, a gas blender 18 is disposed directly adjacent to and in fluid communication with the gas sensor 16. The gas blender 18 is also in fluid communication with the atmosphere or a source and sink of respiratory gases. The gas blender 18 can also be connected to a ventilator or source of calibrated or known gases such as an external oxygen tank 30. The gas blender 18 is preferably computer controlled and is in electrical communication with the computation unit 20 through a conductive line 32. That is, the computation unit 20 can transmit signals to the gas blender 18 in order to modify, mix, or change the composition of the inhaled air passing through the cardiac output analyzer 10 to the subject. In other words, the gas blender 18 can be caused to allow an increase/decrease in the concentration of airway oxygen for a given or predetermined period of time.

In a further alternative embodiment, the pulse oximeter 26 can be replaced by a synchronized, side-port sampling oxygen sensor as is well known in the art. That is, a portion or sample of the gases flowing through the analyzer is directed via a port to an oxygen sensor.

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the formula:

The analyzer 10 can also incorporate an artificial nose and/or a bacterial filter as described in Applicant's previous patents or can incorporate a temperature sensor which provides a signal to the computation unit 20 to adjust the measurements as a function of breath and external air temperature.

In operation, in order to non-invasively obtain a measurement of the cardiac output of a subject, the subject attaches the pulse oximeter 22 to a suitable portion of their body such as a finger or earlobe, the subject then places the mouthpiece 12 into their mouth and the oxygen consumption (VO₂) is determined as the integral of the flow of oxygen concentration signals over an entire breath. The arterial oxygen concentration is calculated according to

$$CaO_2 = (SaO_2)(Hbg)(1.36) + (0.0031)(PaO_2)$$

where SaO₂ is the oxygen saturation measurement obtained by the pulse oximeter 22, Hbg is the hemoglobin concentration (which is entered as a known value or obtained by direct measurement), and PaO₂ is the dissolved arterial oxygen concentration. After obtaining a stable measurement of VO₂ and CaO₂ over a first time period of approximately two to three minutes, the gas blender 18 is caused to increase/decrease the concentration of oxygen (preferably, at least a 10% change in FIO₂, e.g., 40% increased to 50%) supplied to the subject for a second time period less than the subject's circulation time of approximately thirty to fifty seconds. VO₂ and CaO₂ are monitored on a breath-by-breath basis during this time period and the cardiac output is then determined. Accordingly, the method and apparatus of the present invention take advantage of the phenomenon that if the oxygen

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concentration of the inspired gas is temporarily increased or decreased, the change in alveolar oxygen concentration will cause a transient uptake or release of oxygen across the pulmonary capillaries thereby resulting in a change in the measured VO₂ and arterial oxygen content (CaO₂). If these parameters are measured during an interval less than the circulation time (i.e., less than approximately thirty to fifty seconds), then the venous oxygen content (CvO₂) can be ignored and the cardiac output of the subject can be calculated based on the equation

$$C.O. = \frac{\Delta VO_2}{\Delta CaO_2}$$

In view of the teaching presented herein, other modifications and variations of the present invention will readily be apparent to those of skill in the art. The discussion and description are illustrative of some embodiments of the present invention, but are not meant to be limitations on the practice thereof. It is the following claims, including all equivalents, which defines the scope of the invention.

Claims

1	1. A respiratory gas analyzer for measuring cardiac output of a					
2	subject, said analyzer comprising:					
3	a respiratory connector operative to be supported in contact with a					
4	subject so as to pass inhaled and exhaled gases as the subject breathes;					
5	a flow sensor operatively connected to said respiratory connector					
6	adapted to generate electrical signals as a function of the volume of gases					
7	which pass therethrough;					
8	an oxygen sensor;					
9	conduits interconnecting said respiratory connector, said flow meter,					
10	and said oxygen sensor;					
1-1	an oximeter; and					
12	a computer for receiving output signals from said flow sensor, said					
13	oxygen sensor, and said oximeter to calculate the differences between inhaled					
14	and exhaled gas volumes.					
1	2. The analyzer of claim 1, wherein said flow meter is a bi-					
2	directional flow meter.					
1	3. The analyzer of claim 2, wherein said bi-directional flow meter					
2	comprises an ultrasonic flow meter.					
1	4. The analyzer of claim 1 further including a gas blender					
2	operatively connected in fluid communication with said conduits.					

I	5. The analyzer of claim 1, wherein said oxygen sensor is a
2	fluorescence quench oxygen sensor.
1	6. The analyzer of claim 1, wherein said oxygen sensor is a side
2	port sampling oxygen sensor.
1	7. The analyzer of claim 1, wherein said respiratory connector is a
2	mouthpiece.
1	8. The analyzer of claim 4, wherein said flow sensor, said oxygen
2	sensor, said oximeter, and said gas blender comprise a mechanism for
3 -	transferring output signals therefrom to said computer/computation unit.
1	9. The analyzer of claim 7, wherein said mechanism comprises a
2	conductive line.
1	10. The analyzer of claim 1, wherein said gas blender is operatively
2	connected to a source of respiratory gas.
1	11. The analyzer of claim 10, wherein said source of respiratory gas
2	is the atmosphere.
-	is the authosphere.

1 12. The analyzer of claim 10, wherein said source of respiratory gas 2 is a source of oxygen.

- 1 13. A method for non-invasive cardiac output measurement of a subject, said method comprising the steps of:
- 3 (a) determining oxygen consumption of a subject;
- 4 (b) determining end-tidal oxygen concentration of the subject; and
- 5 (c) calculating the cardiac output of the subject based on the oxygen 6 consumption and the end-tidal oxygen concentration determined in steps (a) 7 and (b).
- 1 14. The method of claim 13, wherein arterial oxygen content is 2 determined in accordance with the equation
- 3 $CvO_2 = (SvO_2)(Hbg)(1.36) + (0.0031)(PvO_2)$
- 4 wherein SaO₂ is the oxygen saturation, Hbg is the hemoglobin concentration,
- 5 and PvO_2 is the dissolved venous plasma oxygen.
- 1 15. The method of claim 13, wherein arterial oxygen content is 2 determined in accordance with the equation
- 3 $CaO_2 = (SaO_2)(Hbg)(1.36) + (PaO_2)(0.0031)$
- 4 wherein SaO₂ is the arterial oxygen saturation, Hbg is the hemoglobin
- 5 concentration, and PaO₂ is the dissolved arterial oxygen concentration.

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A method for non-invasive cardiac output measurement of a

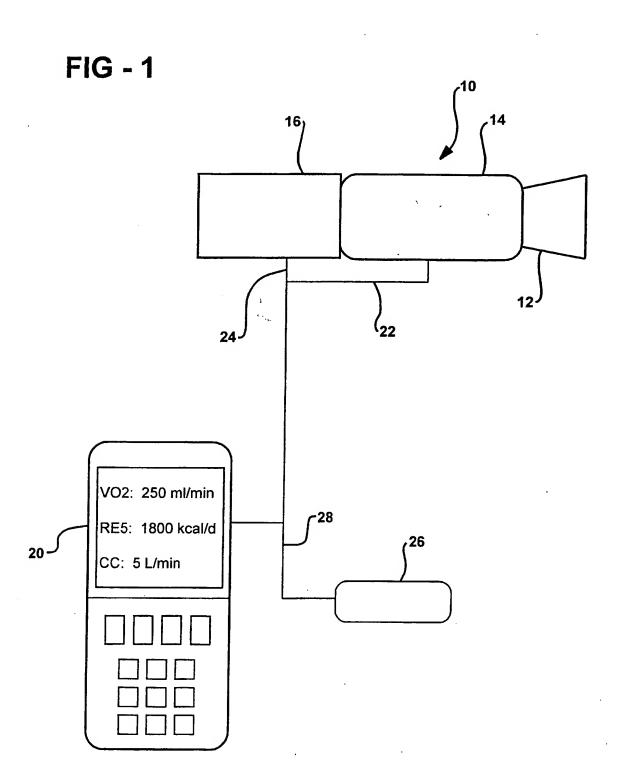
2	subject, said method comprising the steps of:
3	(a) determining oxygen consumption and arterial oxygen content or
4	a subject over a first time interval and for a first oxygen concentration;
5	(b) increasing the oxygen concentration breathed by the subject for
6	a second time interval wherein the second time interval is less than the
7	circulation time of the subject; and
8	(c) calculating the cardiac output of the subject based on the
9	relative change in both oxygen consumption and arterial oxygen content
10	determined in steps (a) and (b).
1	17. The method of claim 16, wherein arterial oxygen content is
2	determined in accordance with the equation
3	$CaO_2 = (SaO_2)(Hbg)(1.36) + (0.0031)(PaO_2)$
4	wherein SaO2 is the oxygen saturation, Hbg is the hemoglobin concentration,
5	and PaO ₂ is end-tidal oxygen concentration in mmHg.
1	18. The method of claim 16, wherein said first time interval ranges
2	from approximately one to five minutes.
1	19. The method of claim 18, wherein said first time interval ranges
2	from approximately two to three minutes.

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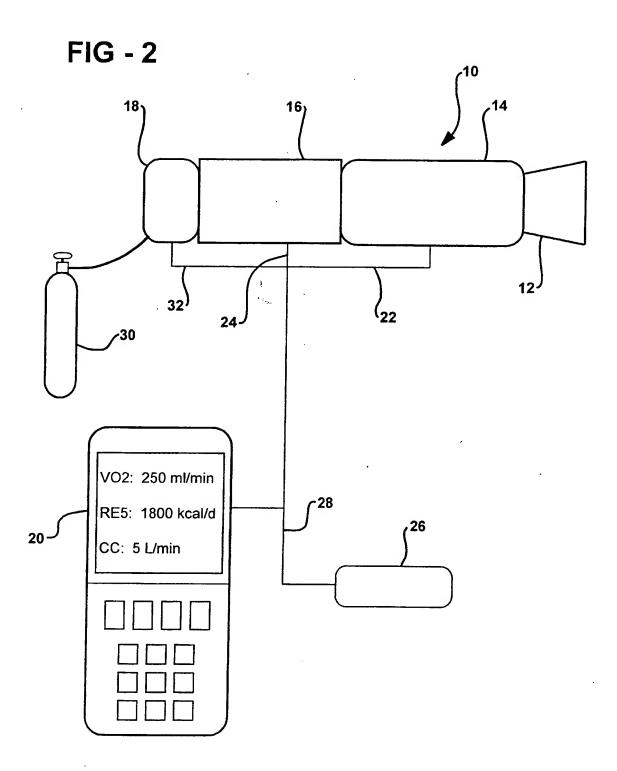
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1	20. The method of claim 16, wherein said second time interval
2	ranges from approximately twenty seconds to sixty seconds.
1 -	21. The method of claim 20, wherein said second time interval
2	ranges from approximately thirty seconds to fifty seconds.
1	22. The method of claim 16, wherein the oxygen concentration in
2	step (b) is increased from approximately 40 percent to approximately 50
3	percent.

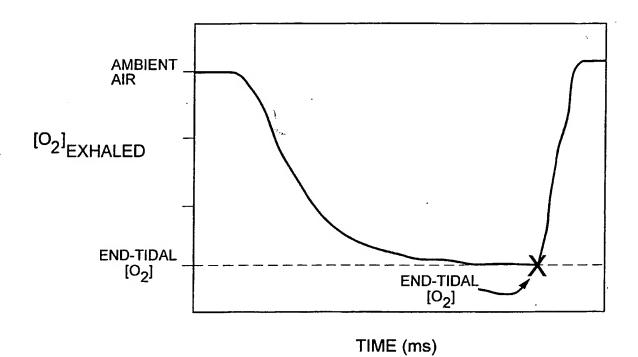


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FIG - 3





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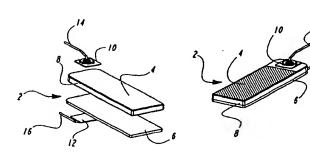
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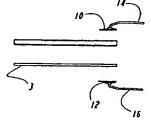
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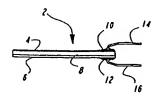
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(54) Title: AIRWAY-BASED CARDIAC OUTPUT MONITOR AND METHODS FOR USING SAME







(57) Abstract: A respiratory gas analyzer (10) for measuring the cardiac output of a subject includes a flow meter (14) and an oxygen sensor (16) interconnected with one another between a mouthpiece (12) and a source of respiratory gases which may be a controlled source or the atmosphere. An oximeter (26) provides measurements of the oxygen saturation of the subject. A computer connected to receive the signals from the flow meter (14), oxygen sensor (16), and oximeter (26) can then calculate the subject's cardiac output.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER IPC(7) :A61B 5/04, 08 US CL :600/526 529 532						
	US CL :600/526, 529, 532 According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELI	DS SEARCHED					
Minimum do	ocumentation searched (classification system followed	d by classification symbols)				
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Documentati	ion searched other than minimum documentation to the	e extent that such documents are included	in the fields searched			
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EAST						
C. DOC	uments considered to be relevant					
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.			
A	US 5,836,300 A (MAULT) 17 Novem	nber 1998, Abstract.	1-22			
A	US 5,355,893 A (MICK et al.) 18 Oc	1-22				
A	US 4,949,724 A (MAHUTTE et al.) 2	1-22				
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10 1	nument defining the general state of the art which is not considered be of particular relevance	principle or theory underlying the inv	carion			
"E" cari	e claimed invention cannot be red to involve an inventive step					
tile	nument which may throw doubts on priority claim(s) or which is to establish the publication date of another citation or other cust reason (as specified)	"Y" document of particular relevance; the				
"Ob the time referring to an oral disclosure, use, exhibition or other means being obvious to a person skilled in the art						
"P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family						
Date of the actual completion of the international search Date of mailing of the international search report 2 3 AUG 2008						
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